

REMARKS

Applicants take this opportunity to thank Examiners Caputa and Yaen for the courtesies extended in the interview on 11/25/02. Following Examiner Caputa's suggestion, claim 49 (to therapy of a human) is incorporated into claim 47, hence the cancellation of claim 49 as moot. As explained by the undersigned, the claims herein had previously been rejected under 35 USC 112, but that rejection has been withdrawn (Paper No. 16, page 3, first paragraph). The only outstanding issue in the case now is a newly raised 103 rejection. The undersigned explained in the interview how the presently claimed methods were patentable over the cited art. Favorable consideration of the present application is respectfully requested in view of the following.

IDSs

Per the request in item 4 on page 2 of the outstanding Office Action, Applicants will have the missing references and clean PTO-1449 forms from the IDSs filed 7/14/99, 12/27/99 and 2/28/01 hand delivered to the Examiner, along with proof of filing. In addition, since the IDS filed 5/21/02 citing references 253-303 is also lost, Applicants will hand deliver a further copy of that IDS for the Examiner's consideration, again along with proof of filing. Consideration of all the cited art, and return of the initialed PTO-1449 forms, is respectfully requested. A Statement of Related Cases is attached. Applicants respectfully request that the Examiner consider the related pending applications with respect to prosecution of the present application.

Section 103

Claims 42, and 44-49 are rejected under 35 USC Section 103 as being unpatentable over Hudziak US Patent 5,770,195 ("the 195 patent") or 5,720,954 ("the '954 patent") and Burton et al. *Am J. Vet Res* 42(2):308-310 (1981).

Applicants submit that the presently claimed invention is patentable over the cited art. Claim 42 herein concerns treating cancer in a mammal comprising administering "subcutaneously" a therapeutically effective amount of a formulation comprising an anti-HER2 antibody in an amount of "about 50mg/mL to about 400mg/mL". Claim 47 concerns treating a human comprising administering a therapeutically effective amount of a stable reconstituted formulation which comprises an anti-HER2 antibody in an amount of "about 50mg/mL to about 400mg/mL", wherein the antibody concentration in the reconstituted formulation is about 2-40 times greater than the antibody concentration in the mixture

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before lyophilization. Claim 48 specifies that the formulation is administered subcutaneously.

Applicants submit that the prior art fails to describe the selection invention herein. With respect to claims 42 and 48, the Examiner has failed to show where the art taught subcutaneous administration of any formulation, let alone subcutaneous administration of a formulation comprising an anti-HER2 antibody. Moreover, claims 42 and 47 herein pertain to therapy with a formulation where the amount of anti-HER2 antibody in the formulation is from about 50mg/mL to about 400mg/mL. On the contrary, the Hudziak patents state that the antibody is typically formulated at concentrations of about 1mg/ml to 10mg/ml (See, the '195 patent at column 12, lines 3-4; and the '954 patent at column 11, lines 61-62).

The present application describes how anti-HER2 antibody formulations can be prepared with high antibody concentrations therein (from about 50mg/mL to about 400mg/mL); see, e.g., Example 1 on pages 25-37. The formulations are especially adapted for subcutaneous (SQ) administration (page 2, lines 16-18) where, in order to achieve the desired dosage, without having to administer a large volume of the formulation SQ, high concentrations of the anti-HER2 antibody in the formulation were desired. The present application demonstrates that the formulations were stable, despite the high protein concentrations therein.

Hence, Applicants submit that the presently claimed invention is patentable over the prior art. Reconsideration and withdrawal of the rejection is respectfully requested.

Respectfully submitted,
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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

47. (Amended) A method for treating a [mammal] human comprising administering a therapeutically effective amount of a stable reconstituted formulation to the [mammal] human in order to treat cancer characterized by overexpression of HER2 receptor in the [mammal] human, wherein the reconstituted formulation comprises an antibody which binds HER2 receptor in an amount of about 50 mg/mL to about 400mg/mL and has been prepared by reconstituting a lyophilized mixture of the antibody and a lyoprotectant in a diluent, wherein the antibody concentration in the reconstituted formulation is about 2-40 times greater than the antibody concentration in the mixture before lyophilization.

Please cancel claim 49, without prejudice or disclaimer.

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Pending Claims as Amended Herein

42. A method for treating cancer characterized by overexpression of HER2 receptor in a mammal comprising administering to the mammal subcutaneously a therapeutically effective amount of a formulation comprising an antibody which binds HER2 receptor in an amount of about 50mg/mL to about 400mg/mL.

44. The method of claim 42 wherein the formulation has been prepared by reconstituting lyophilized antibody in a diluent.

45. The method of claim 42 wherein the mammal is a human.

46. The method of claim 42 wherein the cancer is selected from the group consisting of breast, ovarian, stomach, endometrial, salivary gland, lung, kidney, colon and bladder cancer.

47. A method for treating a human comprising administering a therapeutically effective amount of a stable reconstituted formulation to the human in order to treat cancer characterized by overexpression of HER2 receptor in the human, wherein the reconstituted formulation comprises an antibody which binds HER2 receptor in an amount of about 50 mg/mL to about 400mg/mL and has been prepared by reconstituting a lyophilized mixture of the antibody and a lyoprotectant in a diluent, wherein the antibody concentration in the reconstituted formulation is about 2-40 times greater than the antibody concentration in the mixture before lyophilization.

48. The method of claim 47 wherein the formulation is administered subcutaneously.